The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

◀ Previous Volume 341:1074-1076 September 30, 1999 Number 14 Next ▶

Transmyocardial Laser Revascularization

To perform transmyocardial laser revascularization, the surgeon exposes the beating heart through a lateral thoracotomy, places a laser (carbon dioxide or holmium) on the epicardial surface of the left ventricle, and applies sufficient energy to create small channels from the epicardial to the endocardial surfaces. During a typical procedure, 10 to 50 such channels are created. Initially, these small, laser-created transmyocardial channels were thought to improve the perfusion of ischemic myocardium by providing it with direct access to oxygen-rich left ventricular blood, but it was subsequently found that the channels quickly occlude after the procedure.[1] Nonetheless, initial observational studies of transmyocardial revascularization in patients with severe angina showed that the procedure improved symptoms. In some studies, the relief of angina was sustained,[2] whereas in others, it was relatively short-lived.[3] The effect of transmyocardial revascularization on myocardial perfusion was also inconsistent, with improved perfusion in some studies[2] and no change in others.[3,4] In most studies, the procedure did not improve regional or global left ventricular function.[4,5,6]

On the basis of these observational assessments, three multicenter, randomized, controlled trials — one in the United Kingdom[7] and two in the United States[8,9] — have now compared transmyocardial revascularization with medical therapy in patients with severe angina for whom balloon angioplasty or bypass grafting was deemed unsuitable. In all three trials, there was an improvement in the frequency and severity of angina after transmyocardial revascularization, although the extent of improvement varied: angina diminished by at least two Canadian Cardiovascular Society (CCS) classes in 34 percent of patients in the British study[7] but in about 75 percent of patients in the U.S. studies.[8,9] Partly on the basis of the results of these and other studies, both the carbon dioxide laser and the holmium laser have recently been approved by the Food and Drug Administration for use in transmyocardial revascularization. In our opinion, however, these apparently impressive results must be viewed with caution, since angina is a subjective condition.

In the two U.S. studies, reported in this issue of the *Journal* by Allen et al.[8] and Frazier et al.,[9] angina was assessed on site by investigators who were presumably enthusiastic about transmyocardial revascularization. In both studies, a blinded, independent assessment of angina was also performed, and the results were reported to be within one CCS class of the on-site results in 80 percent of patients. Unfortunately, neither report delineates how often the independent and on-site assessors agreed that angina had improved by two or more classes. Since the actual results of the independent assessment are not provided, one wonders whether it was as favorable as the on-site assessment.

The placebo effect of a thoracotomy should not be underestimated, particularly in patients for whom all therapeutic options have been exhausted and particularly when the procedure is combined with the use of a laser device. In all three trials,[7,8,9] patients were eligible for enrollment only if they had severe, activity-limiting angina despite aggressive antianginal medical therapy and only if bypass grafting and percutaneous revascularization were considered impossible. Many such patients are eager to embrace any procedure that offers hope of improvement. For laypersons and physicians alike, the word "laser" is synonymous with state-of-the-art, successful therapy. This inherent prejudice in favor of laser therapy is impossible to quantify. In the two studies presented in the *Journal* [8,9] 32 percent and 59 percent of the patients initially assigned to receive only medical treatment were crossed over to transmyocardial revascularization. Frazier et al. state that "crossover was allowed as an incentive for patients assigned to maximal medical therapy to remain in the study if medical therapy failed,"[9] which implies a bias on the part of investigators that transmyocardial revascularization was more effective than medical therapy. If transmyocardial revascularization had been thought to be less effective or to be associated with greater morbidity than medical treatment, it would not have been offered as an enticement for patients to remain enrolled. The effect of such a bias may be substantial in a study in which the administration of therapy is not blinded and the crossover of patients is allowed if a subjective end point (in this case, angina) is reached. When the patient or the physician believes that the patient is not receiving the better therapy (transmyocardial revascularization), the likelihood increases that the alternative treatment (medical therapy) will be declared a failure. In short, the success or failure of antianginal medical therapy is a subjective assessment. Before the use of transmyocardial revascularization is embraced enthusiastically, objective evidence of its efficacy should be strong.

Unfortunately, there is little objective evidence that the results of transmyocardial revascularization are superior to those of medical therapy in patients with severe angina. In the study by Allen et al.,[8] the patients treated with transmyocardial revascularization had better exercise tolerance 12 months after enrollment than those treated medically. However, exercise tolerance was measured in fewer than one third of the patients and was not measured before enrollment to establish that the two groups were similar in this respect. In the single study[7] in which exercise tolerance was assessed routinely at enrollment and at 12 months, transmyocardial revascularization was not associated with improvement. In all three trials, myocardial perfusion was assessed at rest and during stress before and at various times after enrollment. In two of the three trials,[7,8] transmyocardial revascularization did not improve myocardial perfusion, and in the third,[9] the magnitude of the improvement in symptoms was disproportionate to the improvement in perfusion. Finally, in none of the three studies was transmyocardial revascularization associated with an improvement in left ventricular systolic function or survival one year after enrollment.

Aside from a potentially marked placebo effect, how might transmyocardial revascularization improve angina? Several mechanisms have been proposed, including proliferation of new blood vessels ("angiogenesis"), denervation of ischemic myocardium, and infarction of ischemic myocardium. In experiments in animals, transmyocardial revascularization induced a highly disorganized pattern of neovascularization at the periphery of laser-created channels that had occluded, a nonspecific response similar to that observed in any scar tissue.[10] Although it has been suggested that neovascularization may improve myocardial blood flow and thereby alleviate angina, the evidence that transmyocardial revascularization improves perfusion of ischemic myocardium is inconsistent and unpersuasive. Improved perfusion of ischemic myocardium achieved by traditional revascularization techniques often leads to improved left ventricular systolic function. However, transmyocardial revascularization does not alter global or regional left ventricular performance.

In studies in dogs, transmyocardial revascularization destroyed cardiac nerve fibers.[11] If this effect occurs in patients, it may explain (at least in part) why myocardial ischemia is often painless in the immediate postoperative period.[12] If, in fact, transmyocardial revascularization compromises the anginal warning system, the advisability of using this procedure is questionable. Finally, perfusion imaging in patients treated with transmyocardial revascularization has not shown a substantial increase in fixed perfusion defects, a change that could suggest the presence of procedure-induced myocardial infarction.[9] However, currently available imaging techniques are not sufficiently sensitive to allow the detection of small laser-induced infarctions. After transmyocardial revascularization, the results of enzymatic tests reveal evidence of myocardial necrosis.

Transmyocardial revascularization is not a risk-free procedure. In the initial observational studies, perioperative mortality was 10 to 20 percent,[2,3,4,5] and it was even higher among patients with severely depressed left ventricular ejection fractions, recent myocardial infarctions, or unstable angina. When such patients are excluded, perioperative mortality is about 5 percent. Perioperative morbidity is considerable: 32 to 68 percent of patients in the current randomized trials[7,8,9] had at least one complication (nonfatal myocardial infarction, congestive heart failure, arrhythmia, or wound or respiratory infection). In addition, the cost of transmyocardial revascularization is likely to be substantial, since the procedure requires expensive laser equipment, operating-room time and staff, the services of a cardiothoracic surgical team, and a relatively long hospital stay. Finally, transmyocardial revascularization is not the only therapeutic option for patients with severe coronary artery disease that is not amenable to traditional revascularization techniques. Recently, novel noninvasive therapies, such as neurostimulation[13] and external balloon counterpulsation,[14] have been shown to improve symptoms and exercise tolerance in such patients. These treatments are associated with lower rates of morbidity and mortality than is transmyocardial revascularization.

Richard A. Lange, M.D.
L. David Hillis, M.D.
University of Texas Southwestern Medical Center
Dallas, TX 75235-9047

References

1. Sigel JE, Abramovich CM, Lytle BW, Ratliff NB. Transmyocardial laser revascularization: three

sequential autopsy cases. J Thorac Cardiovasc Surg 1998;115:1381-1385.[Full Text]
2. Horvath KA, Mannting F, Cummings N, Shernan SK, Cohn LH. Transmyocardial laser revascularization: operative techniques and clinical results at two years. J Thorac Cardiovasc Surg 1996;111:1047-1053.[Abstract/Full Text]
3. Nagele H, Stubbe HM, Nienaber C, Rodiger W. Results of transmyocardial laser revascularization in non-revascularizable coronary artery disease after 3 years follow-up. Eur Heart J 1998;19:1525-1530.[Abstract/Full Text]
4. Agarwal R, Ajit M, Kurian VM, Rajan S, Arumugam SB, Cherian KM. Transmyocardial laser revascularization: early results and 1-year follow-up. Ann Thorac Surg 1999;67:432-436.[Abstract/Full Text]
5. Cooley DA, Frazier OH, Kadipasaoglu KA, et al. Transmyocardial laser revascularization: clinical experience with twelve-month follow-up. J Thorac Cardiovasc Surg 1996;111:791-797.[Abstract/Full Text]
6. Frazier OH, Cooley DA, Kadipasaoglu KA, et al. Myocardial revascularization with laser: preliminary findings. Circulation 1995;92:Suppl II:II-58.
7. Schofield PM, Sharples LD, Caine N, et al. Transmyocardial laser revascularisation in patients with refractory angina: a randomised controlled trial. Lancet 1999;353:519-524. [Erratum, Lancet 1999;353:1714.][CrossRef][Medline]
8. Allen KB, Dowling RD, Fudge TL, et al. Comparison of transmyocardial revascularization with medical therapy in patients with refractory angina. N Engl J Med 1999;341:1029-1036.[Abstract/Full Text]
9. Frazier OH, March RJ, Horvath KA. Transmyocardial revascularization with a carbon dioxide laser in patients with end-stage coronary artery disease. N Engl J Med 1999;341:1021-1028.[Abstract/Full Text]
10. Hughes GC, Lowe JE, Kypson AP, et al. Neovascularization after transmyocardial laser revascularization in a model of chronic ischemia. Ann Thorac Surg 1998;66:2029-2036.[Abstract/Full Text]
11. Kwong KF, Schuessler RB, Kanellopoulos GK, Saffitz JE, Sundt TM III. Nontransmural laser treatment incompletely denervates canine myocardium. Circulation 1998;98:Suppl II:II-67.
12. Hughes GC, Landolfo KP, Lowe JE, Coleman RB, Donovan CL. Diagnosis, incidence, and clinical significance of early postoperative ischemia after transmyocardial laser revascularization. Am Heart J 1999;137:1163-1168.[Medline]
13. Mannheimer C, Eliasson T, Augustinsson LE, et al. Electrical stimulation versus coronary artery bypass surgery in severe angina pectoris: the ESBY study. Circulation 1998;97:1157-1163.[Abstract/Full Text]
14. Arora RR, Chou TM, Jain D, et al. The multicenter study of enhanced external counterpulsation (MUST-EECP): effect of EECP on exercise-induced myocardial ischemia and anginal episodes. J Am Coll Cardiol 1999;33:1833-1840.[CrossRef][Medline]

This article has been cited by other articles:

- Thadani, U. (2004). Current Medical Management of Chronic Stable Angina. *J CARDIOVASC PHARMACOL THER* 9: S11-S29 [Abstract]
- Kim, M. C., Kini, A., Sharma, S. K. (2002). Refractory angina pectoris: Mechanism and therapeutic options. *JACC* 39: 923-

934 [Abstract] [Full Text]